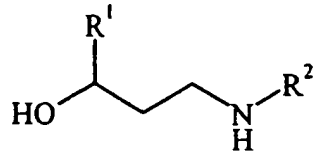
Claims

1. A process for the preparation of a compound of formula

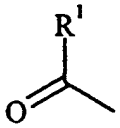


I

and/or an addition salt of a proton acid, wherein R^1 and R^2 independently represent alkyl, cycloalkyl, aryl or aralkyl, each aryl or aralkyl being optionally further substituted with alkyl, alkoxy and/or halogen, which process comprises the following steps

a) reacting a mixture comprising

(i) a methyl ketone of formula



IV

wherein R^1 is as defined above, and

(ii) a compound of formula

$H_2N—R^2$ V

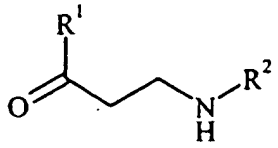
and/or an addition salt of proton acid, wherein R^2 is as defined above, and

(iii) formaldehyde or a source of formaldehyde selected from the group consisting of formaldehyde in aqueous solution, 1,3,5-trioxane, paraformaldehyde and mixtures thereof, in the presence of

a solvent selected from the group consisting of water, aliphatic alcohols, cycloaliphatic alcohols and mixtures thereof, and

optionally a proton acid

to afford a β-amino ketone of formula



II

and/or an addition salt of a proton acid, and

b) reducing the carbonyl group of said β-amino ketone to afford a compound of formula I, and/or an addition salt of a proton acid

wherein the first step is carried out at a pressure above 1.5 bar.

2. The process of claim 1 wherein R^1 is selected from the group consisting of linear or branched C_{1-8} alkyl, C_{3-8} cycloalkyl, phenyl, naphthyl, furanyl, benzofuranyl, thienyl, benzo[b]thienyl and aralkyl, wherein the alkyl moiety of the aralkyl residue is linear C_{1-4} alkyl, and the aryl moiety is selected from the group consisting of phenyl, naphthyl, furanyl, benzofuranyl, thienyl and benzo[b]thienyl,
each aryl or aralkyl being optionally substituted with halogen, linear or branched C_{1-4} alkyl, linear or branched C_{1-4} alkoxy, C_{3-6} cycloalkyl, CF_3, C_2F_5, OCF_3 or OC_2F_5.

3. The process of claim 1 or 2 wherein R^2 is selected from the group consisting of linear or branched C_{1-8} alkyl, C_{3-8} cycloalkyl, phenyl, naphthyl, furanyl, benzofuranyl, thienyl, benzo[b]thienyl and aralkyl, wherein the alkyl moiety of the aralkyl residue is linear C_{1-4} alkyl, and the aryl moiety is selected from the group consisting of phenyl, naphthyl, furanyl, benzofuranyl, thienyl and benzo[b]thienyl,
each aryl or aralkyl being optionally substituted with halogen, linear or branched C_{1-4} alkyl, linear or branched C_{1-4} alkoxy, C_{3-6} cycloalkyl, CF_3, C_2F_5, OCF_3 or OC_2F_5.

4. The process of any of claims 1 to 3, wherein the compound of formula V is present in an amount at least equimolar to that of the compound of formula IV.

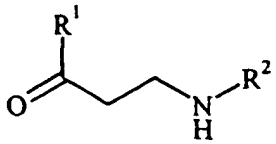
5. The process of any of claims 1 to 4, wherein the proton acid is a carboxylic or an inorganic acid, the acid being preferably selected from the group consisting of formic acid, acetic acid, propionic acid, oxalic acid, malonic acid, benzoic acid, HF, HCl, HBr, HI, H_2SO_4, H_3PO_4, mono alkali malonate, alkali hydrogensulfates, alkali hydrogenphosphates and alkali hydrogencarbonates.

6. The process of any of claims 1 to 5, wherein aliphatic and cycloaliphatic alcohols are selected from the group selected of linear or branched aliphatic C_{1-12} alcohols, cycloaliphatic C_{5-8} alcohols, di- and/or triethylene glycols and mono C_{1-4} alkyl or acetyl derivatives thereof, each of said alcohols containing 1 to 3 hydroxy groups.

7. The process of claim 6, wherein the alcohol is selected from the group consisting of methanol, ethanol, propanol, isopropyl alcohol, butanol, isobutanol, *tert*-butanol, 1-pentanol, 2-pentanol, 3-pentanol, 1-hexanol, 2-hexanol, cyclopentanol, cyclohexanol, 1,2-ethanediol, 1,2-propanediol, 1,2-butanediol, 2,3-butanediol, 1,4-butanediol, 1,2,3-propanetriol, 1,2,6-hexanetriol, diethylene glycol, diethylene glycol monomethyl ether, diethylene glycol monoethyl ether, diethylene glycol monobutyl ether, diethylene glycol monoacetate, triethylene glycol, triethylene glycol monomethyl ether, triethylene glycol monoethyl ether, triethylene glycol monobutyl ether and triethylene glycol monoacetate.

8. The process of any of claims 1 to 7, wherein the pressure during reaction step a) is above 1.5 bar, more preferably in the range of 1.5 to 10 bar and more particularly preferred in the range of 1.5 to 5 bar.

9. A compound of formula

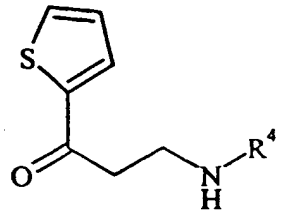


II

and its addition salts of proton acids, wherein R^1 represents
furanyl, benzofuranyl, isobenzofuranyl, thienyl or benzo[b]thienyl,
each being optionally substituted with halogen, linear or branched C_{1-4} alkyl, linear or branched C_{1-4} alkoxy, C_{3-6} cycloalkyl, CF_3, C_2F_5, OCF_3 or OC_2F_5; and
wherein R^2 is selected from the group consisting of
linear or branched C_{1-8} alkyl, C_{3-8} cycloalkyl, phenyl, naphthyl, furanyl, benzofuranyl, thienyl, benzo[b]thienyl and aralkyl, wherein the alkyl moiety of the aralkyl residue is linear C_{1-4} alkyl, and the aryl moiety is selected from the group consisting of phenyl,

naphthyl, furanyl, benzofuranyl, thienyl and benzo[b]thienyl,
each aryl or aralkyl being optionally substituted with halogen, linear or branched C_{1-4} alkyl, linear or branched C_{1-4} alkoxy, C_{3-6} cycloalkyl, CF_3, C_2F_5, OCF_3 or OC_2F_5 with the exception of the compound wherein R^1 represents thienyl and R^2 represents benzyl.

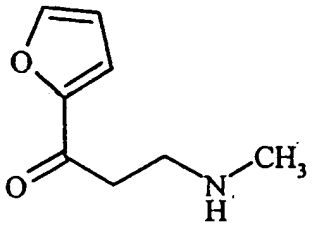
10. A compound of formula



VI

and its addition salts of proton acids, wherein R^4 represents methyl, ethyl, isobutyl or *tert*-butyl.

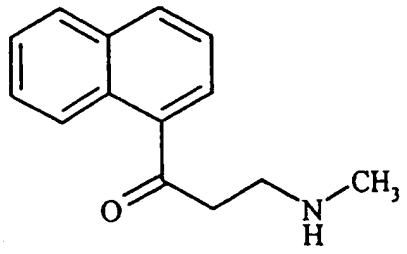
11. A compound of formula



VII

and its addition salts of proton acids.

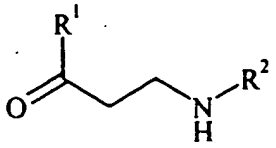
12. A compound of formula



VIII

and its addition salts of proton acids.

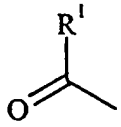
13. A process for the preparation of a compound of formula



II

and/or an addition salt of a proton acid, wherein R^1 and R^2 independently represent alkyl, cycloalkyl, aryl or aralkyl, each being optionally further substituted with alkyl, alkoxy and/or halogen, which process comprises reacting

(i) a methyl ketone of formula



IV

wherein R^1 is as defined above, and

(ii) a compound of formula

$H_2N—R^2$ V

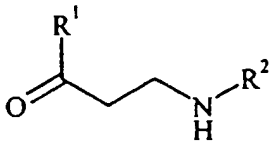
and/or an addition salt of a proton acid, wherein R^2 is as defined above, and

(iii) formaldehyde or a source of formaldehyde selected from the group consisting of formaldehyde in aqueous solution, 1,3,5-trioxane, paraformaldehyde and mixtures thereof, in the presence of

a solvent selected from the group consisting of water, aliphatic alcohols, cycloaliphatic alcohols and mixtures thereof, and

optionally a proton acid

to afford a β-amino ketone of formula



II

and/or an addition salt of a proton acid, wherein R^1 and R^2 are as defined above, and

wherein the reaction is carried out at a pressure above 1.5 bar.

14. The process of claim 13 wherein R^1 is as defined in claim 2.

15. The process of claim 13 or 14 wherein R^2 is as defined in claim 3.

16. The process of any of claims 13 to 15, wherein the compound of formula V is present in an amount at least equimolar to that of the compound of formula IV.

17. The process of any of claims 13 to 16, wherein the proton acid is a carboxylic or an inorganic acid, preferably the acid is selected from the group consisting of formic acid, acetic acid, propionic acid, oxalic acid, malonic acid, benzoic acid, HF, HCl, HBr, HI, H_2SO_4, H_3PO_4, mono alkali malonate, alkali hydrogensulfates, alkali hydrogenphosphates and alkali hydrogencarbonates.

18. The process of any of claims 16 to 17, wherein aliphatic and cycloaliphatic alcohols are selected from the group consisting of linear or branched aliphatic C_{1-12} alcohols, cycloaliphatic C_{5-8} alcohols, di- triethylene glycols and mono C_{1-4} alkyl or acetyl derivatives thereof, each of said alcohols containing 1 to 3 hydroxy groups.

19. The process of claim 18, wherein the alcohol is selected from the group consisting of methanol, ethanol, propanol, isopropyl alcohol, butanol, isobutanol, *tert*-butanol, 1-pentanol, 2-pentanol, 3-pentanol, 1-hexanol, 2-hexanol, cyclopentanol, cyclohexanol, 1,2-ethanediol, 1,2-propanediol, 1,2-butanediol, 2,3-butanediol, 1,4-butanediol, 1,2,3-propanetriol, 1,2,6-hexanetriol, diethylene glycol; diethylene glycol monomethyl ether, diethylene glycol monoethyl ether, diethylene glycol monobutyl ether, diethylene glycol monoacetate, triethylene glycol, triethylene glycol monomethyl ether, triethylene glycol monoethyl ether, triethylene glycol monobutyl ether and triethylene glycol monoacetate.

20. The process of any of claims 13 to 19, wherein the pressure during the reaction is above 1.5 bar, more preferably in the range of 1.5 to 10 bar and more particularly preferred in the range of 1.5 to 5 bar.